April 20, 1970

Dr. John Totter
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Atomic Energy Commission
Washington, D. C. 20545

3-18-70

Dear John:

JOHN TOTTER

Thank you for having arranged my meeting with the Commission last month. It was an opportunity I welcomed very much and I really did enjoy the discussion. Thank you also for arranging the various materials I have been receiving and will digest as rapidly as I can.

I did want to respond with an amplification of Part II of the minutes dated April 2, 1970 having to do with Jim Cleaver's work. I feel that this represents such an extraordinary opportunity for assaying radiation (and other environmental mutagenic) effects in vivo that I ought to get the proposal on the record with some amplification and precision. The proposed assay is based on the work that Cleaver did with xeroderma, but it would be applied to cells taken from randomly selected bloods - perhaps even as a by-product of routine blood bank collections. These would then be genetically normal individuals. The assay is based on the concept that Cleaver has worked out a method to determine the rate of DNA repair. For his studies to date he has used material intentionally insulted with UV in order to examine genetic defects in the capacity for repair. But he has also been able to measure repair in untreated cells,and this presumably represents the response to the background level of DNA damage and should be proportional to it. One should, then, be able to detect changes in the rate of DNA damage after acute exposure to mutagenic agents, even if their effect is of the same order of magnitude as the background.

So I then would see two lines to further research exploiting this possibility: (1) the examination of cells from experimental animals and humans known to have been exposed to specific low doses of radiation, and (2) a population survey to look for variations in the rate of DNA repair (and therefore presumably DNA damage) that might be correlated with various environmental factors. For example, one might really be able to get after the question of an altitude effect in terms of specific biological response. I am even more stimulated by the idea of verifying hazards from chemical environmental additives.

Sincerely yours,

Joshua Lederberg
Professor of Genetics